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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,913	02/05/2004	Steven W. Dow	86715.0002	5237

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,913	DOW ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-20,24-31,50-53 and 56-67* is/are pending in the application.

4a) Of the above claim(s) *7-16,18-20,50-53 and 56-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,24-31,66 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement..

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 10/9/07 has been entered. Claims 1-6, 21-23, 32-49, and 54-55 are canceled. Claims 7-20, 24-31, 50-53 and 56-67 are currently pending in the instant application. Of these, claim 8 was withdrawn from prosecution in the previous office action.

In the instant amendment, the applicant has amended claims 7, 9-16, 18-20, 50-53, and 56-65 such that these claims no longer read on the elected invention. As discussed in the previous office action, applicant's initial response to the restriction requirement received on 11/14/06 elected Invention II. However, applicant's supplemental response received on 11/20/06 stated that the supplemental response was intended to supersede the previous response, see page 1 of the response. This supplemental response elected Invention IV without traverse. Group IV, as set forth in the restriction requirement mailed on 9/21/06, is drawn to methods of eliciting a tumor antigen specific immune response comprising administering a liposome delivery vehicle and total RNA isolated from a tumor sample. Claims 7, 9-16, 18-20, 50-53, and 56-65 now recite a composition comprising a liposome delivery vehicle and non-coding RNA, or methods of eliciting a systemic, non-specific immune response comprising administering a liposome delivery vehicle and non-coding RNA. The subject matter in amended claims 7, 9-16, 18-20, 50-53, and 56-65 does not correspond to the subject matter of Group IV, as the method steps utilize materially different reagents for different purposes. In particular, note that total RNA derived from a tumor contains numerous coding RNA species for a large number of proteins, including tumor specific antigens. The coding RNA derived from the tumor and the non-coding RNA of

the amended claims further have different modes of operation and function, and exhibit different effects, i.e. the induction of tumor specific, versus, non-specific immune responses. It is further noted that the subject matter of amended claims 7, 9-16, 18-20, 50-53, and 56-65 does not correspond to any of the originally claimed subject matter subject to restriction in the requirement mailed on 9/21/06. Thus, for the reasons discussed above, had the subject matter of amended claims 7, 9-16, 18-20, 50-53, and 56-65 been originally presented, it would have been restricted from the invention of Group IV. Therefore, claims 7, 9-16, 18-20, 50-53, and 56-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention , there being no allowable generic or linking claim.

This application therefore contains claims 7-16, 18-20, 50-53, and 56-65 drawn to an invention nonelected without traverse in the reply filed on 11/20/06 which are now withdrawn from prosecution.

Claims 17, 24-31, and 66-67 are currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Priority

Applicant's amendment of the first page of the specification to update the status of parent application 09/104,759 is acknowledged.

Claim Rejections - 35 USC § 112

The rejection of claims 7, 9-20, 24-31, 50-53 under 35 U.S.C. 112, first paragraph, for scope of enablement is withdrawn over amended claims 7, 9-16, 18-20, and 50-53 as these claims are no longer drawn to the elected subject matter and have been withdrawn from prosecution, and further withdrawn over claims 17, and 24-31 in view of the amendments which have deleted the limitations of preventing or eliminating cancer, or cancer metastases, and in view of applicant's arguments.

The rejection of claims 7-10 and 66-67 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn over amended claims 7-10 as these claims are no longer drawn to the elected subject matter and have been withdrawn from prosecution, and maintained over claims 66-67.

Claims 66-67 have been amended to depend on claim 27 and to further recite that the method "further comprises converting said total RNA into a plurality of cDNA sequences amplified from said total RNA and operatively linking each of said cDNA sequences to a transcription control sequence". The applicant argues that these amendments clarifies the invention by setting forth that the method includes the additional step of converting the RNA to cDNA. The claim amendments and applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection of record. Although claims 66-67 now depend on claim 27 instead of claim 50, claim 27, like claim 50 before, recites a method comprising the administration of a therapeutic composition comprising a liposome and total RNA derived from a tumor cell. Claims 66-67 seek to further limit claim 27, however, the

limitations in amended claims 66-67 conflict with the limitations of claim 27. As indicated, claim 27 is drawn to the administration of total RNA. Claims 66-67 now add the step of converting the RNA to cDNA. As discussed in the previous office action, cDNA is DNA, not RNA, and each is comprised of different molecules, i.e. deoxyribonucleic acids versus ribonucleic acids. Thus, if the RNA is converted to cDNA, how can the method continue to comprise administration of total RNA as set forth in claim 27. As such, the claims as written contain conflicting limitations that render the claims confusing in that it is unclear whether the applicant intends to administer RNA or cDNA in the methods as claimed. Thus, the metes and bounds of the claims cannot be determined. It is also reiterated that the elected invention is drawn to liposomes and total RNA. If applicant intends to claim methods and/or compositions comprising liposomes and cDNA, such claims would be subject to restriction and, based on the instant examination of the elected invention of liposomes and RNA, would be withdrawn from prosecution.

Claim Rejections - 35 USC § 102

The rejection of claims 56, 60, 63 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,670,186 (2003), hereafter referred to as Nair et al., is withdrawn as claims 56, 60, and 63 have been amended such that they no longer recite the elected subject matter and have been withdrawn from prosecution.

Claim Rejections - 35 USC § 103

The rejection of claims 7, 9-20, 24, 26, 28-30, 50-53, 56-61, and 63-64 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,589,466 (1996), hereafter referred to as Felgner et al., in view of U.S. Patent No. 6,670,186 (2003), hereafter referred to as Nair et al., is withdrawn over claims 7, 9-16, 18-20, 50-53, and 56-61 as these claims are no longer drawn to the elected subject matter and have been withdrawn from prosecution, and further withdrawn over claims 17, 24, 26, and 28-30 in view of applicant's amendments to these claims to depend on either claims 25 or 27. However, please note that these claims have been newly rejected under 35 U.S.C. 103 below.

Claims 17, and 24-31 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,589,466 (1996), hereafter referred to as Felgner et al., in view of U.S. Patent No. 6,670,186 (2003), hereafter referred to as Nair et al., and U.S. Patent No. 6,977,073 (2005), hereafter referred to as Cezayirli et al. Please note that applicant's arguments made in reference to the teachings of Felgner et al. and Nair et al. have been addressed as they pertain to this new rejection, see below following the rejection of record.

Felgner et al. teaches methods of immunizing a mammal by administering a preparation comprising a cationic liposome containing an mRNA encoding an immunogenic peptide, wherein the expression of the immunogen in the cells of a mammal induces immune responses, including humoral and cellular immune responses, including cytotoxic T lymphocytes (CTL) (Felgner et al., columns 7-9, 20-22, 25-26, and 29-32, especially columns 8-9, bridging paragraph, and examples 7-9). In particular, Felgner et al. teaches that the immunogenic peptide is associated with a tumor and induces CTL capable of killing the tumor (Felgner et al., column

8). Felgner et al. further teaches that the preparation can include a nucleic acid encoding a cytokine, and preferably one of the interferons (Felgner et al., column 8 and columns 22-23, bridging paragraph). Felgner et al. also teaches that cationic liposomes can be unilamellar or multilammelar, formed from cationic lipids such as DOTMA, or DOTAP, and other materials such as cholesterol (Felgner et al., columns 25-26). In addition, Felgner et al. teaches that routes of administration of the peptide include intravenous administration and administration to a body cavity (Felgner et al., column 7, and column 32- example 9 for intravenous administration of mRNA/liposomes). Felgner et al. also teaches the inclusion of nonionic materials such as sugars in the preparations (Felgner et al., columns 23, and 32). Felgner et al. further teaches that the ratio of mRNA to liposome can vary, and exemplifies one ratio of 1:40 mRNA to cationic liposomes (Felgner et al., column 30).

Felgner et al. differs from the instant invention by teaching the use of a single mRNA immunogen associated with a tumor instead of total tumor RNA or total tumor mRNA. Nair et al. supplements Felgner et al. by teaching RNA/cationic liposome compositions useful for transfecting cells in order to stimulate immune responses where the RNA is total RNA or polyA+RNA derived from a tumor, i.e. mRNA (Nair et al., columns 1-5, especially column 5). Nair et al. provides motivation for using total tumor RNA and especially total tumor mRNA by teaching that the use of RNA enriched tumor preparations circumvents the need to isolate and identify a tumor antigen, has the capacity to elicit immune responses against multiple tumor antigens, thus reducing escape mutants, and extends the immunotherapy methods to tumors in which specific tumor antigens have not been identified (Nair et al., columns 1 and 6). Nair et al. further teaches that the RNA can be derived from tumors such as melanomas, breast cancer,

prostate cancer, bladder cancer, pancreatic cancer, colon cancer, and ovarian cancer (Nair et al., column 3). Cezayirli et al. further supplements the teachings of Felgner et al. and Nair et al. by teachings that in order to induce multivalent vaccination against cancers such as lung cancer, antigen presenting cells such as dendritic cells can be contacted with a representative sample of different allogeneic tumor RNAs, such as the combination of tumor RNAs from progressive stages of the same cancer type (Cezayirli et al., columns 4-6). Cezayirli et al. further provides motivation for using a plurality of RNAs from tumor of the same histological type by teaching that by using a combination of RNAs representing various differentiation periods in the disease state progression a vaccine can be produced that may protect against a whole spectrum of a specified cancer (Cezayirli et al., column 4, lines 44-67).

Thus, based on the motivation provided by Nair et al. for using total tumor RNA or total tumor mRNA over isolated RNA encoding a tumor antigen in methods to stimulate anti-tumor immune responses, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize total tumor RNA or mRNA derived from tumors such as melanomas or colon carcinomas instead of a single mRNA encoding a tumor antigen in the methods of stimulating immune responses in a mammal taught by Felgner et al. In addition, based on the motivation to combine RNAs from different stages of a tumor type in order to vaccinate against a spectrum of differentiation states of a cancer, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize a mixture of total tumor RNAs from allogeneic tumors of a specified type in different stages of differentiation instead of a single mRNA or total tumor RNA from a single tumor cell in the methods of stimulating immune responses in a mammal taught by Felgner et al. Further, the skilled artisan would have had a reasonable expectation of success in

using total tumor RNA or total tumor mRNA and cationic liposomes to generate anti-tumor immune responses in view of the successful use by Felgner of mRNA/cationic liposomes to induce immune responses when administered intravenously and the successful use by Nair et al. of total tumor RNA/cationic liposomes to transfect cells.

Applicant's arguments regarding Felgner et al. and Nair et al. are addressed as they pertain to the new grounds of rejection presented above. The applicant argues that claims 17, 24, 26, and 28-30 have been amended to depend on either claim 25 or 27, and that neither of claims 25 or 27 was rejected over the combination of Felgner et al. and Nair et al. In response, the new rejection set forth above is based on the combined teachings of Felgner et al., Nair et al., and Cezayirli et al. and includes rejection of independent claims 25 and 27 and dependent claims 17, 24, 26, and 28-31. As such, applicant's arguments are not found persuasive.

The rejection of claim 62 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,589,466 (1996), hereafter referred to as Felgner et al., in view of U.S. Patent No. 6,670,186 (2003), hereafter referred to as Nair et al., and further in view of U.S. Patent No. 5,830,878 (11/3/98), hereafter referred to as Gorman et al., is withdrawn

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all

official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633